

**CARDIOVASCULAR DISEASE MORBIDITY AND
MORTALITY AND ITS RELATIONSHIP WITH RISK
FACTORS IN KELANTAN POPULATION**

by

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LIST OF ABBREVIATIONS

BMI	Body Mass Index
CI	Confidence Interval
cm	centimeter
dl	deciliter
ECG	Electrocardiogram
HDL	High Density Lipoprotein
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
kg	kilogram
l	liter
LDL	Low Density Lipoprotein
m	meter
mg	milligram
ml	milliliter
mm	millimeter
mmHg	millimeter mercury
mmol	millimol
OR	Odds Ratio
WHR	Waist Hip Ratio

MORBIDITI DAN MORTALITI PENYAKIT KARDIOVASKULAR DAN HUBUNG KAITNYA DENGAN FAKTOR-FAKTOR RISIKO DI KALANGAN PENDUDUK KELANTAN

ABSTRAK

Objektif kajian ini adalah untuk mengenalpasti insiden penyakit kardiovaskular dan menyiasat hubungkaitnya dengan faktor-faktor risiko penyakit kardiovaskular di kalangan penduduk Kelantan. Kajian ini merupakan kajian retrospektif kohort di mana kaedah persampelan kelompok multi-tahap digunakan. Kohort seramai 1710 subjek adalah daripada kajian keratan rentas yang telah dilaksanakan pada tahun 1992. Seramai 911 (53.3%) subjek dapat dikesan dan menyertai kajian ini. Selebihnya, seramai 249 (14.6%) subjek telah meninggal dunia dan 550 (32.3%) lagi tidak dapat dikesan. Data asas individu mengenai risiko penyakit kardiovaskular telah dikumpulkan ketika kohort ini mula-mula diperiksa. Morbiditi penyakit kardiovaskular, iaitu kes-kes yang tidak membawa maut (kes-kes penyakit jantung koronari dan penyakit serebrovaskular) dinilai menggunakan soalan soal selidik Rose dan status bebas strok. Mortaliti dinilai menggunakan soalan soal selidik WHO autopsi lisan.

Sebanyak 580 kejadian kardiovaskular diperoleh sepanjang 12 tahun pemeriksaan susulan ke atas 1160 subjek. Morbiditi penyakit kardiovaskular sebanyak 460 dikenalpasti daripada 911 subjek. Kadar insiden kumulatif bagi penyakit jantung koronari ialah 315 per 1000 dan 337 per 1000 bagi penyakit serebrovaskular. Sebanyak 120 mortaliti penyakit kardiovaskular dikenalpasti daripada 249 kematian dengan 78 kematian disebabkan oleh penyakit jantung koronari dan 42 disebabkan oleh penyakit serebrovaskular. Kadar

kematian penyakit kardiovaskular adalah 48.2% daripada semua kematian. Kajian ini menunjukkan perokok mempunyai risiko yang lebih tinggi untuk mengalami kejadian kardiovaskular (penyesuaian OR: 1.37; 95% CI: 1.03-1.79) dan morbiditi penyakit jantung koronari (penyesuaian OR: 1.40; 95% CI: 1.00-1.97) berbanding bukan perokok. Lelaki mempunyai risiko yang lebih tinggi untuk menghidap penyakit kardiovaskular (penyesuaian OR: 1.39; 95% CI: 1.02-1.88) dan penyakit serebrovaskular (penyesuaian OR: 1.47; 95% CI: 1.09-2.02) berbanding wanita. Tekanan darah sistolik berkadar langsung terhadap mortaliti kardiovaskular (penyesuaian OR: 1.02; 95% CI: 1.01-1.03). Trigliserida juga berkadar langsung terhadap mortaliti kardiovaskular (penyesuaian OR: 1.72; 95% CI: 1.20-2.48) dan penyakit serebrovaskular (penyesuaian OR: 1.27; 95% CI: 1.03-1.56) tetapi berkadar songsang terhadap morbiditi penyakit kardiovaskular (penyesuaian OR: 0.85; 95% CI: 0.74-0.98).

Kajian ini juga dijalankan untuk memantau evolusi faktor-faktor risiko penyakit kardiovaskular dalam jangkamasa 12 tahun. Di kalangan mereka yang tidak mempunyai faktor-faktor risiko penyakit kardiovaskular pada peringkat awal, 198 (43.5%) mengalami hipertensi, 97 (13.5%) mengalami diabetes, 23 (4.5%) mengalami obesiti, 145 (37.4%) mengalami hiperkolesterolemia dan 68 (11.3%) mengalami peningkatan kolesterol lipoprotein berketumpatan rendah selepas 12 tahun. Ini mewakili sebanyak 3.6% kadar pertukaran per tahun untuk hipertensi, 1.1% untuk diabetes, 0.4% untuk obesiti, 3.1% untuk hiperkolesterolemia dan 0.9% untuk peningkatan kolesterol lipoprotein berketumpatan rendah. Subjek yang mengalami prahipertensi dan berat badan berlebihan pada peringkat awal telah menunjukkan risiko untuk mengalami hipertensi dan obesiti sebanyak 4.7% dan 3.3% per tahun, masing-masing. Kadar pertukaran kepada diabetes untuk subjek yang mengalami gangguan toleransi berpuasa (GTP) dan gangguan toleransi glukosa (GTG)

pada peringkat awal adalah sebanyak 2.1% dan 1.9% per tahun, masing-masing. Peramal untuk setiap faktor-faktor risiko penyakit kardiovaskular juga dikenalpasti. Umur dan tekanan darah sistolik berkadar langsung terhadap pertukaran daripada tekanan darah normal kepada hipertensi. Wanita mempunyai risiko yang lebih tinggi untuk mendapat hipertensi daripada tekanan darah normal. Tekanan darah diastolik, glukosa berpuasa dan trigliserida berkadar langsung terhadap pertukaran daripada normal glukosa kepada diabetes. Walaubagaimanapun, umur berkadar songsang terhadap pertukaran daripada normal glukosa kepada diabetes. Indeks jisim tubuh (IJT) berkadar langsung terhadap pertukaran daripada GTG kepada diabetes. Walaubagaimanapun, umur berkadar songsang terhadap pertukaran daripada normal IJT kepada obesiti. Wanita mempunyai risiko yang lebih tinggi untuk mendapat hiperkolesterolemia berbanding lelaki. Kolesterol lipoprotein berketumpatan rendah berkadar langsung terhadap risiko hiperkolesterolemia. Total kolesterol berkadar langsung terhadap risiko peningkatan kolesterol lipoprotein berketumpatan rendah.

Kesimpulannya, perokok mempunyai risiko yang lebih tinggi untuk mengalami kejadian kardiovaskular berbanding bukan perokok. Lelaki mempunyai risiko yang lebih tinggi untuk menghidap penyakit kardiovaskular daripada wanita. Trigliserida dan tekanan darah sistolik berkadar langsung terhadap mortaliti kardiovaskular. Oleh itu, usaha-usaha dalam pencegahan dan pengawalan penyakit kardiovaskular dan faktor-faktor risikonya di Kelantan haruslah mengambil kira penemuan ini.

CARDIOVASCULAR DISEASE MORBIDITY AND MORTALITY AND ITS RELATIONSHIP WITH RISK FACTORS IN KELANTAN POPULATION

ABSTRACT

Objectives of this study were to determine the incidence of cardiovascular disease and investigate its associations with cardiovascular risk factors in the Kelantan population. This study was a retrospective cohort study with a multistage cluster sampling design. A cohort of 1710 people identified in a previous cross-sectional study in 1992 was followed up. There were 911 (53.3%) subjects traceable and participated in this study. Of the rest, 249 (14.6%) have died and 550 (32.2%) were untraceable. Individual baseline data on cardiovascular risk factors had been collected when the cohort was first examined 12 years earlier. Cardiovascular disease morbidity, that is, the occurrence of non-fatal events (cases of coronary heart disease and cerebrovascular disease) was assessed using Rose and stroke-free status questionnaire. The mortality was assessed by WHO verbal autopsy questionnaire.

A total of 580 cardiovascular events developed after 12-years follow-up of 1160 subjects. There were 460 cardiovascular disease morbidity identified from 911 subjects. Cumulative incidence rate for coronary heart disease was found to be 315 per 1000 and 337 per 1000 for cerebrovascular disease. There were 120 deaths from cardiovascular disease identified among 249 recorded deaths, 78 deaths due to coronary heart disease and 42 due to cerebrovascular disease. Cardiovascular mortality rate was found to be 48.2% of all deaths. This study showed that smokers had a higher risk of developing total cardiovascular events (adjusted OR: 1.37; 95% CI: 1.03-1.79) and coronary heart disease morbidity

(adjusted OR: 1.40; 95% CI: 1.00-1.97) compared to non-smokers. Males had a higher risk of developing cardiovascular morbidity (adjusted OR: 1.39; 95% CI: 1.02-1.88) and cerebrovascular disease morbidity (adjusted OR: 1.47; 95% CI: 1.09-2.02) compared to females. Systolic blood pressure positively predicted cardiovascular mortality (adjusted OR: 1.02; 95% CI: 1.01-1.03). Triglyceride positively predicted the risk for cardiovascular mortality (adjusted OR: 1.72; 95% CI: 1.20-2.48) and cerebrovascular disease mortality (adjusted OR: 1.27; 95% CI: 1.03-1.56) but, negatively predicted the risk for cardiovascular disease morbidity (adjusted OR: 0.85; 95% CI: 0.74-0.98).

This study was also conducted to observe the evolution of cardiovascular risk factors over a 12-year period. Among subjects who did not have risk factors at baseline, 198 (43.5%) developed hypertension, 97 (13.5%) developed diabetes, 23 (4.5%) developed obesity, 145 (37.4%) developed hypercholesterolemia and 68 (11.3%) developed elevated LDL cholesterol after 12 years of follow-up. This represented a 3.6% of conversion rate per year for hypertension, 1.1% for diabetes, 0.4% for obesity, 3.1% for hypercholesterolemia and 0.9% for elevated LDL cholesterol. Subjects with prehypertension and overweight at baseline have been shown to have a risk of developing hypertension and obesity of 4.7% and 3.3% per year, respectively. The conversion rates of progression to diabetes for subjects with IFG and IGT at baseline were 2.1% and 1.9% per year, respectively. Predictors of progression to each cardiovascular risk factor were identified. Age and systolic blood pressure positively predicted the progression from baseline normal blood pressure and prehypertension to hypertension. Diastolic blood pressure positively predicted the progression from baseline prehypertension to hypertension. Females had a higher risk of developing hypertension from baseline normal blood pressure. Diastolic blood pressure, fasting blood glucose and triglyceride positively predicted the progression from normal

blood glucose to diabetes. Age negatively predicted the progression from baseline normal blood glucose to diabetes. Body mass index (BMI) positively predicted the progression from baseline IGT to diabetes. Age negatively predicted the progression from baseline normal BMI to obesity. Female had a higher risk of getting hypercholesterolemia compared to male. LDL cholesterol positively predicted the risk for hypercholesterolemia. Total cholesterol positively predicted the risk for elevated LDL cholesterol.

In conclusion, smokers had a higher risk of developing total cardiovascular events compared to non-smokers. Males had a higher risk of developing cardiovascular morbidity than females. Triglyceride and systolic blood pressure significantly predicted the risk for cardiovascular mortality. Therefore, efforts in the prevention and control of cardiovascular disease and its risk factors in Kelantan should take into consideration these findings.

CHAPTER 1: INTRODUCTION

1.1 LITERATURE REVIEW

1.1.1 Global burden of non-communicable diseases

Non-communicable diseases especially cardiovascular diseases are a major disease burden in the world. By 2020, non-communicable diseases including cardiovascular diseases are predicted to account for seven out of every ten deaths in developing countries (Khor, 2001). Many risk factors for cardiovascular diseases are related to common lifestyle determinants such as physical inactivity, low fruit and vegetable intake, high fast food consumption, and high cholesterol intake. These risk factors are predominant causes of non-communicable diseases not only cardiovascular diseases but also cancers, diabetes, and chronic obstructive pulmonary disease (Khatib, 2004).

Among non-communicable diseases, special attention has been devoted to cardiovascular diseases, diabetes, cancer, and chronic pulmonary diseases. Their burden is affecting countries worldwide with a growing trend in developing countries (Boutayeb and Boutayeb, 2005). The current burden of non-communicable diseases was highlighted by the estimates provided in the Global Burden of Disease Study and in the World Health Report, which indicate that these diseases contributed to 59% of global mortality (31.7 million deaths) and 43% of the global burden of disease in 1998 (Yusuf *et al.*, 2001a).

1.1.2 Overview of cardiovascular diseases

Cardiovascular diseases are a group of disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, peripheral vascular disease, heart failure, rheumatic heart disease, congenital heart disease, and cardiomyopathies (Boutayeb and Boutayeb, 2005).

The major cardiovascular risk factors such as overweight, central obesity, high blood pressure, diabetes mellitus, and hypercholesterolemia greatly contribute to the development of cardiovascular disease (Reddy, 2002). Many of these risk factors are associated with unhealthy eating habits, socio-economic pressure, smoking and decreased physical activities (Lam and Khor, 1997).

1.1.3 Global burden of cardiovascular diseases

The pattern of cardiovascular epidemic may vary within a country by geography and socioeconomic status. Developed countries with rapid social and economic development may become one of the earliest countries facing rapid increment in cardiovascular diseases and have a higher prevalence of cardiovascular diseases than developing countries. The transition of cardiovascular diseases from being diseases of the wealthy to the poor have been documented in the United Kingdom and the United States (Marmot *et al.*, 1991). For example, cardiovascular diseases were relatively rare in the African-American community in the 1960s but now its incidence equals or exceeds that in the white population of the United State (National Heart, Lung and Blood Institute, 1999). A similar pattern is appearing in some parts of India where demographic projections suggest a major increase in cardiovascular diseases mortality as life expectancy increases

and the age structure of the growing population changes. Surveys in urban areas also suggest that coronary risk factors are already widespread and that urgent action is needed to prevent a further rise as socioeconomic development proceeds (Reddy, 1993).

Cardiovascular diseases are a major contributor to the global burden of disease among the non-communicable disease and are the leading cause of death in the developing countries. World Health Organization (WHO) estimated that cardiovascular diseases accounted for 29.3% of all deaths in the developing countries in 2001 (World Health Organization, 2002). According to the Global Burden of Disease Study, a 55% rise would occur in cardiovascular disease mortality between 1990 and 2020 in the developing countries. This would be in contrast to a 14.3% reduction in the contribution of cardiovascular disease-related deaths during the same period in the developed countries. For example, cardiovascular related deaths in India are expected to rise from 24.2% in 1990 to 41.8% of total deaths in 2020 (Murray and Lopez, 1996). This phenomenon is evident in Latin America, parts of Africa, China, and India. Thus, the increasing mortality trend of cardiovascular diseases would be borne mostly by the developing countries in the next two decades.

Cardiovascular deaths in 1998 contributed to 34% of global mortality in women and 28.2% of all deaths in men (World Health Organization, 1999). Such scenario also exists within the developing countries, where women are increasingly affected by hypertension, stroke, and coronary heart disease. As the epidemics advance, the social gradient also reverses with the poor becoming the most vulnerable victim in both developed and developing countries (Reddy and Yusuf, 1998). Risk behaviors, risk factors, and disease

burdens in the developed countries were initially higher in the population with high social classes. However, these factors became a mass phenomenon as the population from high social classes reduced their risk in response to new knowledge and technologies (Reddy, 2002). This is evident from studies in India which showed that non-educated and less educated people in rural India have a higher prevalence of coronary heart disease and of the coronary risk factors such as smoking and hypertension (Gupta *et al.*, 1994).

The epidemiologic transition also resulted in a decrease of deaths in childhood due to infections but with a concomitant increase in cardiovascular and other chronic diseases. Thus in 1990, 46.7% of cardiovascular diseases related deaths in developing countries occurred below the age of 70 years, in contrast to only 22.8% in the high income industrial countries. The Global Burden of Disease Study projected that 6.4 million deaths would occur due to cardiovascular diseases in the developing countries in 2020, in the age group of 30 to 69 years (Reddy, 2002). Between 1990 and 2020, the increase in ischemic heart disease mortality is 120% in women and a 137% in men in the developing countries. This is greater than predicted for the developed countries; 29% and 48% respectively. A similar pattern for increases in cerebrovascular disease mortality was also predicted by others; 124% and 107% increases among men and women in developing countries versus 78% and 56% increases respectively, in the developed countries (Yusuf *et al.*, 2001a). These projections are largely based on changes in the demographics of the population and have not yet taken into account potential increases in risk factor prevalence.

1.1.4 Cardiovascular diseases mortality trends in the Asia Pacific region

Cardiovascular diseases in the Asia Pacific region ranges from less than 20% of total deaths from all causes in countries such as Thailand, Philippines and, Indonesia to 20 to 30% in Hong Kong, Japan, Korea, Malaysia, and urban China. Countries such as New Zealand, Australia, and Singapore have relatively high prevalence of cardiovascular diseases that exceeds 30 to 35%. Countries like New Zealand, Australia, and Singapore also show the highest prevalence of mortality from coronary heart disease which is more than 150 deaths per 100,000. However, the mortality rate associated with cerebrovascular disease remains low in South-east Asian countries including Thailand, Malaysia, Indonesia, and Philippines which is below 20 per 100,000 (Khor, 2001). Eastern stroke and coronary heart disease collaborative research study reported that death from cerebrovascular disease ranks higher in East Asian countries including Japan, China, and Taiwan which is more than 100 deaths per 100,000 than New Zealand and Australia which is 50 to 80 per 100,000 (Eastern Stroke and Coronary Heart Disease Collaborative Research Group, 1998).

It is worth noting that developed countries in the Asia Pacific region with high proportions of deaths from cardiovascular diseases have undergone marked declining rates in recent decades. For example, mortality from coronary heart disease in Australian men and women aged 30 to 69 years declined by 46% and 51% respectively between 1989 and 1996 (Sexton and Sexton, 2000). Meanwhile, countries in the region with high mortality rates for cerebrovascular disease such as Japan and Singapore also have undergone rapid decreases. In Japan, age-adjusted mortality from cerebrovascular disease declined 70% while that from coronary heart disease decline by 20%. The cerebrovascular disease mortality rate in Japan dropped from a high level of 150 per 100,000 during the 1920 to

approximately 100 per 100,000 in 1940 (Iso *et al.*, 1999).

On the other hand, cardiovascular diseases mortality is reported to be on the rise in developing or newly developed countries in the region including China, Malaysia, Korea, and Taiwan (Sekikawa *et al.*, 1999). These countries are at different stages of epidemiological transition accompanied by rapid changes in dietary practices and lifestyles behavior. In China, cardiovascular diseases mortality increased as a proportion of total deaths from 12.8% in 1957 to 35.8% in 1990 (Yao *et al.*, 1993). The figures reported by WHO in 1998 for the cardiovascular disease proportion of total deaths in urban China is 37% for men and 41% for women, while the figures for rural men and women are 29% and 32%, respectively. Rapid pace of economic development and industrialization in China in the past two decades has brought about rapid changes in lifestyles including a shift towards westernization of dietary patterns, especially in urban areas (Guo *et al.*, 1999). Thus, monitoring the impact of these changes on cardiovascular risk factors is essential to enable the implementation of appropriate strategies towards countering the rise of mortality from cardiovascular diseases.

1.1.5 Variations in cardiovascular diseases rate by the epidemiologic transition, ethnicity and impact of urbanization

Several factors may contribute to the differences in the cardiovascular diseases profile. At any given time, different countries in the world or even different regions within a country are at different stages of the epidemiologic transition. This epidemiologic transition has resulted in a decrease in deaths in childhood due to infections, with a concomitant increase in cardiovascular and other chronic disease (Omran, 1971). Thus, the

total burden of cardiovascular diseases will vary according to the dynamics of health transition. Environmental factors related to cardiovascular diseases risk differ widely across populations and may be partly related to culture as well as stage of urbanization. The rates of urbanization are increasing globally, from 36.6% of the world population living in urban areas in 1970 to 44.8% in 1994. This proportion is projected to increase to 61.1% by 2025 (MacLean and Chockalingam, 1999). With urbanization or migration to westernized environments, there is a marked increase in consumption of energy rich foods, a decrease in energy expenditure as well as less physical activity and a loss of the traditional social support mechanisms. In addition to increased migration of individuals from rural to urban areas, rural areas are themselves also being transformed. For example, increased mechanization in agriculture and increased use of automobile and bus transportation in rural areas are leading to a decrease in physical activity. Concomitantly, global influences via television or increased availability of processed food on lifestyles perceived to be desirable or modern are changing the types of food consumed in both urban and rural areas (Yusuf *et al.*, 2001a).

Ethnicity encompasses both genetic and cultural differences (Anand, 1999). Because individuals of different ethnic backgrounds tend to live in distinct regions and societies, variations in disease rates by ethnicity are elicited with geographic differences. Furthermore, specific ethnic groups within one location adopt certain lifestyle, whereas the same ethnic groups in another location may adopt substantially different lifestyles. For example in the Seven Countries Study, low coronary heart disease rates were observed in Japan and the Mediterranean countries and high coronary heart disease rates in Finland and the United States. These differences were explained by differences in diet, serum

cholesterol and blood pressure (Menotti *et al.*, 1993).

Genetic factors also explained variance in the risk of incidence for cardiovascular diseases within populations by providing the basis for differences in individual susceptibility in a shared and relatively homogenous environment. They also contribute to interpopulation differences, due to variable frequencies of one or more genetic determinants of risk in different ethnic groups. Genetic contributions to lipid disorders, obesity, salt sensitivity, insulin resistance, coagulation derangements, and endothelial dysfunction are being explored (Goldbourt *et al.*, 1994).

The effect of programming factors may also determine individual responses to environmental challenges and thereby contribute to the differences of cardiovascular disease in population. The thrifty gene hypothesis has been postulated to be a factor in promoting selective survival of persons who encountered an adverse environment of limited nutritional resources (Hales and Barker, 1992). Other programming factors which may underlie population differences in coronary heart disease are the state of intrauterine, infant and early childhood nutrition (Barker, 1994). An adverse intrauterine growth environment due to poor maternal nutrition may confer a selective survival advantage to the fetus that has been programmed for reduced insulin sensitivity. However, as the child is exposed to over nutrition in later childhood and early adulthood, such programming could lead to high blood pressure, glucose intolerance and dyslipidaemia. It has been suggested improving intrauterine growth may modify the susceptibility of South Asians to diabetes.

Variations in cardiovascular disease between different populations are illustrated by the knowledge gained from studies in migrant groups, where environmental changes due to altered lifestyles are superimposed over genetic influences. The classical Ni-Hon-San study of Japanese migrants revealed how blood cholesterol levels and coronary heart disease rates rose from relatively low levels among those in Japan, to intermediate levels in Honolulu and to high levels in San Francisco (Kagan *et al.*, 1974). Comparison of Afro-Caribbeans, South Asians and Europeans in the United Kingdom indicate marked differences in central obesity, glucose intolerance and dyslipidaemia despite similar blood pressure, body mass index and total plasma cholesterol (McKeigue *et al.*, 1991). In Canada, there are marked differences between different ethnic groups in the prevalence and deaths from coronary heart disease with the highest rates being among those of Chinese origin. There was a greater rate of clinical events among South Asians compared with European and Chinese (11%, 5% and 2%, respectively) for similar degrees of atherosclerosis, suggesting that the propensity to plaque rupture may vary in different ethnic groups (Anand *et al.*, 2000).

Therefore, epidemiologic transitions, urbanization, ethnicity, geographic region and early childhood programming influences as well as differences in gene frequency or expression can contribute to variations in cardiovascular diseases rates between parts of the world (Yusuf *et al.*, 2001a).

1.1.6 Variations in cardiovascular diseases by geographic regions, ethnic groups, risk factors and prevention strategies

Most countries in the world have experienced great transitions in social structures, economics, politics, education, and home environments over the 20th century. This has resulted in a shift from agricultural and rural societies to industrial and urban societies.

These social and economic transitions have resulted in major changes in population demography, industrial structure, income levels, expenditure patterns, education levels, family structures, eating habits, and physical activity. These changes have markedly increased cardiovascular risk factors and disease rates (Yusuf *et al.*, 2001b).

Data from the WHO indicate that the cardiovascular disease mortality rate is 6-fold higher among men and women in the Russian Federation compared with people in France. In 1996, the age-standardized mortality rate for coronary heart disease among males in the Russian Federation was 390 per 100,000 compared with 60 per 100,000 among males in France. The age-standardized mortality rate for cerebrovascular disease was 244 per 100,000 among males in the Russian Federation compared with 40 per 100,000 in France (World Health Organization, 2000). Eastern European countries such as the Ukraine, the Russian Federation, Hungary and the Czech Republic have the highest and increasing cardiovascular diseases rates in the world. This is in contrast to most economically stable European countries where declines in cardiovascular diseases mortality rate have been experienced over the past 30 years. The risk factors attributed to the epidemic of cardiovascular diseases in Eastern European countries are partly related to high levels of smoking and excessive alcohol consumption as well as with diets high in saturated fat and poor social conditions (Marmot, 1995). Studies to explain why the Italian and French populations remain relatively protected from coronary heart disease have led to numerous hypotheses. It is believed that the high consumption of monounsaturated fats such as olive oil and antioxidants may be responsible for the low rates of coronary heart disease in Italy. In France, the coronary heart disease mortality rate remains very low (Artaud-Wild *et al.*, 1993). The relative protection from coronary heart disease has been attributed to high

consumption of red wine (Criqui and Ringel, 1994). Others however believe that the lower rate of coronary heart disease mortality may be due to a time-lag between increases in consumption of animal fat and elevations in serum cholesterol concentrations and resulting increases in heart disease which have occurred later (Law and Wald, 1999).

Cardiovascular diseases rate in Japan have declined more markedly than those of western countries and the life expectancy is also among the highest in the world parallel with a rise in economic prosperity. Mortality rates from coronary heart disease have traditionally been much lower in Japan than in western countries. The age-standardized mortality rates for coronary heart disease in males is 43 per 100,000 and in females is 22 per 100,000 which is one-fourth the rate of coronary heart disease in North America. For cerebrovascular disease it is 72 per 100,000 and 46 per 100,000 among males and females, respectively (World Health Organization, 2000). This pattern of higher cerebrovascular disease compared with coronary heart disease among Japanese differs from western populations (Shimamoto *et al.*, 1989). Hypertension is the most important of cardiovascular risk factor among Japanese more so than cholesterol and cigarette smoking. The Hisayama prospective population based study showed a decline in blood pressure level from 1961 to 1987, likely due to improved diagnosis and treatment of hypertension (Fujishima *et al.*, 1992). This has been accompanied by a marked decline in cerebrovascular disease mortality. Low serum cholesterol related to a diet low in saturated fat and cholesterol is also likely responsible for the low rates of coronary heart disease mortality observed in the Japanese. The prevalence of diabetes mellitus in Japanese males (13%) and females (9%) is higher than the rates in most western countries (Fujishima *et al.*, 1996). Between 1961 to 1987, with westernization, there was a 2 to 3-fold increase in glucose intolerance, diabetes

melitus, obesity, and hypercholesterolemia (Ohmura *et al.*, 1993). It is possible that as cholesterol and glucose levels rise, the impact of high cigarette smoking rates on cardiovascular diseases may manifest as an increased rate.

Death rates from cardiovascular diseases particularly coronary heart disease have been increasing in China in recent decades (Woo and Donnan, 1989). Although the cardiovascular diseases mortality rate in China is approximately the same as that in the United States, the coronary heart disease mortality rates are approximately 50% lower than the rates observed in most western countries and the cerebrovascular disease rate is significantly higher. In 1996, in urban China, the age-standardized mortality rates for coronary heart disease for men and women aged 35 to 74 was 100 per 100,000 in men and was 69 per 100,000 in women. However, the age-standardized mortality rate for cerebrovascular disease in men and women aged 35 to 74 was 251 per 100,000 in men and 170 per 100,000 in women (World Health Organization, 1998). Intracerebral hemorrhage occurs between 2 and 3 times more frequently in the Chinese than in white Caucasian populations. Only 6% to 12% of cerebrovascular disease in European populations are reported as intracerebral hemorrhages compared with 25% to 30% of hemorrhagic cerebrovascular disease in Chinese (Thorvaldsen *et al.*, 1995). A case-control study from Hong Kong of acute myocardial infarction indicates that conventional risk factors such as cigarette smoking, hypertension and diabetes are important (Donnan *et al.*, 1994). Although the mean serum cholesterol among Chinese is low (mean 4.2 mmol/L at baseline) by western standards, serum cholesterol was directly related to coronary heart disease mortality even at relatively low levels (Chen *et al.*, 1991). Cigarette smoking is increasing and highly prevalent among Chinese men (63%) than women (3.8%) (Yang *et al.*, 1999).

There are relatively few mortality studies from India as there is no uniform completion of death certificates and no centralized death registry for cardiovascular disease (Reddy, 1993). However, the WHO and the World Bank estimate that death attributable to cardiovascular disease has increased in parallel with the expanding population in India. The coronary heart disease mortality rate is also expected to rise in parallel with the increase in life expectancy which has increased from 41 years in the years 1951 to 1961, to 61.4 years in the years 1991 to 1996 and is projected to reach 72 years by 2030, which could lead to large increases in cardiovascular disease prevalence (Reddy and Yusuf, 1998). South Asians in the Canada and United Kingdom do not display high rates of smoking, hypertension or elevated cholesterol but still have higher rates of coronary heart disease compared with the Europeans. They also suffer a high prevalence of impaired glucose tolerance (IGT), central obesity, elevated triglycerides, and low high density lipoprotein (HDL) cholesterol (Anand *et al.*, 2000). However, smoking, hypertension, and diabetes are strongly associated with coronary heart disease among South Asians in India (Pais *et al.*, 1996). Moreover adverse changes in cardiovascular risk factors and disease rates are observed when South Asians adopt an urban lifestyle whether they live in India or abroad. South Asians in the United Kingdom have higher risk factor levels compared with their siblings living in India with body mass index (BMI), 27 versus 23 kg/m²; systolic blood pressure, 144 versus 137 mm Hg; total cholesterol, 6.3 versus 5.0 mmol/L; lower HDL cholesterol, 1.14 versus 1.27 mmol/L and higher fasting glucose, 5.4 versus 4.6 mmol/L) (Bhatnagar *et al.*, 1995).

An earlier study suggested that the age-adjusted mortality rates for cardiovascular diseases among Mexican-Americans were 28.8 and 26.6 per 100,000 men and women,

respectively which were lower than those of African-Americans (40.5 and 39.6, respectively) and whites (30.0 and 23.8 per 100,000) (Becker *et al.*, 1988). However, more recent data from the Corpus Christi Heart Project reported that there was a greater incidence of myocardial infarction in Mexican-Americans compared with non-Hispanic whites (Goff *et al.*, 1997). The age-adjusted incidence for ischemic heart disease was higher by 1.25 and 1.52 among Mexican-American men and women compared with non-Hispanic whites (Stern *et al.*, 1987). Hispanics aged below 65 years have a significantly elevated cerebrovascular disease death rate compared with non-Hispanic whites which was 32 versus 19 and 23 versus 18 per 100,000 in men and women respectively. However, at the ages 65 and over the cerebrovascular disease rate in Hispanics is substantially lower than whites which is 589 versus 765 per 100,000 in men and 535 versus 847 per 100,000 in women (Gillum, 1995). Although declines in coronary heart disease and cerebrovascular disease mortality have occurred in Mexican-Americans over the past 20 years, this decline has been less than that which has occurred among non-Hispanic whites (Stern *et al.*, 1987). Cardiovascular risk factors such as smoking, diabetes, high cholesterol, and hypertension were important predictors and positively associated with cardiovascular diseases mortality in Mexican Americans. These risk factors accounted for 55% of cardiovascular diseases mortality compared with 46% in non-Hispanic whites (Wei *et al.*, 1996).

1.1.7 Cardiovascular events and the risk factors in Singapore

Cardiovascular diseases mortality rate in Singapore have increased from 1968 to 1984 compared with other countries such as Japan, New Zealand, and Australia (Beaglehole *et al.*, 1988). A study found that mortality in coronary heart disease in Indians was three times that of Chinese and that for Malays was 1.5 times more than that of

Chinese in Singapore (Emmanuel, 1989). In another study on mortality and morbidity of cardiovascular diseases in Singapore, the mortality of coronary heart disease was three times more common in Indians compared to other ethnic groups (Chen, 1980). A more recent study also showed that Indians have a higher mortality for ischemic heart disease than Malays and Chinese. However, Malays had the highest mortality for hypertensive disease and there was no significant difference in mortality from the cerebrovascular disease in the different ethnic groups in Singapore (Hughes *et al.*, 1990a). A prospective cohort study in Singapore has shown that the incidence of ischemic heart disease is 3.8 per 1,000 person-years and 1.8 per 1,000 person-years for cerebrovascular disease. This study also found that Indians had the highest risk of getting ischemic heart disease compared to Malays and Chinese in both sexes. Meanwhile, Chinese and Indian males had a higher incidence for cerebrovascular disease than Malays but there were not statistically significant. However, the risk to get cerebrovascular disease was highest among Malay females being 2.57 times of that of Chinese females (Heng *et al.*, 2000).

Several risk factors contributing to the development of coronary heart disease have been identified among Singaporeans. These include a high level of fat consumption, high serum cholesterol, glucose intolerance, high blood pressure, cigarette smoking, and obesity. The 1992 Singapore National Health Survey was conducted among 3,568 respondents found that the prevalence of diabetes between 18 and 69 years of age was 8.4%, with 12.2% in Indians, 10.1% in Malays and 7.8% in Chinese. More than half (58.5%) of the total diabetic individuals were previously undiagnosed (Tan *et al.*, 1999). The evaluation of the National Healthy Lifestyle Program was carried out in 1998 by the Singapore National Health Survey to determine whether the risk factors in the population had changed. The

1998 results suggest that the National Healthy Lifestyle Program significantly decreased the prevalence of regular cigarette smoking (at least once a day) from 18.4% to 15.0% between 1992 and 1998. The proportion of Singaporeans who exercised regularly (at least three times a week for at least 20 minutes per session) increased from 13.6% to 16.9% between 1992 and 1998. Meanwhile, the prevalence of obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) was unchanged being 5.1% in 1992 and 5.9% in 1998, so was diabetes mellitus; 8.4% in 1992 and 8.1% in 1998. However, the prevalence of high total blood cholesterol ($\geq 6.2 \text{ mmol/l}$) increased from 19% in 1992 to 23.5% in 1998 and the prevalence of hypertension was also increased from 22.5% in 1992 to 26.6% in 1998. Ethnic differences were also observed in the prevalence of all cardiovascular risk factors studied among the three major ethnic groups namely Chinese, Malays, and Indians. Indians had the highest prevalence of diabetes mellitus with 14.5% followed by Malays (10.7%) and Chinese (7.0%), while Malays had the highest prevalence (32.3%) of hypertension compared with Chinese (26.0%) and Indians (23.7%). Obesity prevalence was low among the Chinese (3.8%), compared to Malays (15.3%) and Indians (12.3%). Malay and Indian women had an especially high prevalence of obesity (22.0% and 17.5%, respectively), compared to Chinese women (3.0%). High total blood cholesterol was more prevalent in Malays (34.0%), compared to Chinese (21.8%) and Indians (23.0%). Malays also had the highest prevalence of cigarette smoking (men: 42.9%; women: 3.7%; Chinese men: 23.4%; Chinese women: 3.3%; Indian men: 29.3%; Indian women: 0.8%). On the other hand, more Indians (25.0%) and Malays (19.3%) exercised regularly compared to Chinese (15.8%) (Cutter *et al.*, 2001).

A study on the differences in cardiovascular risk factors among the three ethnic groups in Singapore showed that the major risk factors such as smoking, blood pressure and serum cholesterol cannot explain the higher mortality from ischemic heart disease found in Indians. It found that cigarette-smoking rate was higher in Malay males with 53.3% followed by Indian (44.5%) and Chinese (37.4%). Malays had higher mean systolic blood pressure than Chinese and Indians in both sexes. There was no ethnic difference for serum cholesterol level, low-density lipoprotein (LDL) cholesterol and triglyceride. Nevertheless, the highest prevalence of diabetes among males was found in Indians followed by Malays and Chinese meanwhile for females it was Malays, followed by Indians and Chinese (Hughes *et al.*, 1990b). Another prospective study in Singapore has investigated the relationships of coronary risk factors with incidence of coronary heart disease for Chinese, Malays and Indians males. The study found that individuals with hypertension or diabetes showed a higher risk of getting coronary heart disease. Meanwhile, high LDL cholesterol, high fasting triglyceride and low HDL cholesterol showed a moderately increased risk of coronary heart disease. Alcohol drinkers were found to be protective with non-drinkers having 1.8 times increased risk of coronary heart disease compared to drinkers. Obesity (BMI ≥ 30) showed an increased risk. An increased risk of coronary heart disease was found in cigarette smokers of ≥ 20 pack years but not with lesser amounts (Lee *et al.*, 2001).

1.1.8 Trends in cardiovascular mortality in Peninsular Malaysia

Cardiovascular diseases are becoming the leading cause of mortality in Malaysia since the early 1970s. Deaths due to cardiovascular diseases increase 16.5 times from 1.8% of total deaths from all causes in 1950 to 29.6% in 1989. This level exceeds the total deaths from respiratory diseases, neoplasms, infectious diseases, metabolic diseases, and blood

diseases. Infectious diseases, which ranked first in the 1950s, had fallen to fourth position in 1989. Coronary heart disease and cerebrovascular diseases has emerged as the main causes of mortality among the four specific cardiovascular diseases. Coronary heart disease deaths increase from 32.7% of all cardiovascular diseases in 1965 to 38.2% in 1989. Similarly, an increase of 3.0% to 11.3% was also found during the same period when compared with the total mortality of all causes. However, mortality due to other forms of cardiovascular diseases have declined, for example cerebrovascular disease fluctuated from 33.1% in 1975 to 30.1% in 1989, rheumatic heart disease dropped from 4.5% in 1965 to 1.7% in 1989 and hypertensive diseases fell from 16.8% in 1965 to 1.4% in 1989. Coronary heart disease occurred more often in males than in females between 1960 and 1980. This trend became less apparent during 1985 until 1989. The changes in this trend could be due to changes in diagnostic pattern as awareness of cardiovascular disease in females may have increased among doctors. Coronary heart disease mortality was highest among Indians followed by Chinese and Malays. Coronary deaths in Indians were about 1.5 to 1.8 times higher than Chinese and Malays. Mortality due to coronary heart disease was higher among the 55 to 59 age groups in 1965. However between 1985 and 1989, it shifted to the older age group of 65 to 69 years of age. This shift in the mode of distribution suggested that there was an improvement in general health and care of ageing population from 1965 to 1989 (Khoo *et al.*, 1991). The findings of the above study were comparable to a study reported by the Registrar General, Malaysia from 1968 to 1971. A study showed that coronary heart disease deaths occurred more often in males than females. Indians have the highest mortality rates compared to Chinese and Malays in both sexes and in all age groups. Coronary heart disease mortality rates in the age group of 30 to 69 years in males were 367.2 per 100,000 populations in Indians, 105.6 per 100,000 in Chinese and 142.3 per

100,000 in Malays. Meanwhile, coronary heart disease mortality rates in the same age groups of females were 74.4 per 100,000 populations in Indians, 33.0 per 100,000 in Malays and 31.2 per 100,000 in Chinese. Mortality due to coronary heart disease was higher in the older age group of 60 to 69 years of age between 1968 to 1971 (Safiah, 1996).

1.1.9 Major cardiovascular risk factors in Malaysia

Studies on the prevalence of cardiovascular risk factors among Malaysians have shown that it is on the increase since the early 1960s. The National Health and Morbidity Survey (NHMS) has been carried out at 10-year intervals, with the first in 1986 and the second survey in 1996. The first NHMS in Peninsular Malaysia was aimed to provide supplementary data that could be used for the development and evaluation of health programs in the country. As a follow-up to the first NHMS, the second NHMS involving a total of 59,903 subjects in Malaysia was conducted 10 years later in 1996 to provide community-based data and information for Ministry of health to review health priorities, program strategies and activities, and planning for the allocation of resources. The second NHMS was extended to Sabah and Sarawak to provide information on health and morbidity status of the whole country.

A national sample for the second NHMS component of blood pressure of 21,391 Malaysian adults aged 30 or older estimated that 32.9% (Lim *et al.*, 2000a) of the individuals exhibited a blood pressure of 140/90 mmHg which is categorized as hypertension. Malay and other indigenous women had the highest prevalence of hypertension while Chinese and Indian women had the lowest prevalence. Among hypertensive, 33% were aware of their hypertension, 23% were currently on treatment and

a mere 6% had controlled hypertension (Lim and Morad, 2004). Meanwhile in a smaller survey done in 1980 involving 963 respondents in Selangor, 14% were found hypertensive and of these, 16.8% were from the urban areas and 12.3% from rural areas. A study reported that Malays (14.7%) had the highest prevalence of hypertension (blood pressure of $\geq 160/95$ mmHg) followed by Chinese (14.5%) and Indians (10.8%) (Kandiah *et al.*, 1980). In a study of 2508 subjects from the state of Kelantan in North-East Peninsular Malaysia found that the overall prevalence of hypertension in Kelantan (mean systolic blood pressure of ≥ 160 mmHg and/or mean diastolic blood pressure ≥ 95 mmHg or on antihypertensive treatment) was 13.9%. There was no difference in the prevalence of hypertension between males and females. Subjects with hypertension also had a higher prevalence of diabetes mellitus (19.0% versus 10.5%), obesity (39.4% versus 25.5%) and hypercholesterolemia (70.7% versus 57.8%) than the non-hypertensive subjects. Other than age, BMI, plasma glucose, total cholesterol and LDL cholesterol, hypertensive subjects also had a higher mean serum urea, creatinine, uric acid and triglyceride than non-hypertensive subjects (Mafauzy *et al.*, 2003) .

Diabetes is also reported to be prevalent in Malaysia. The second NHMS component on blood glucose was conducted among 20,028 Malaysian adults aged 30 years and above demonstrated that 8.3% showed 2 hours post blood glucose levels exceeding 11.1 mmol/l, 4.3% in the IGT range (2 hours post blood glucose concentration ≤ 11.1 and ≥ 7.8 mmol/l) and 87.4% in the normal range (2 hours post blood glucose concentration ≤ 7.8 mmol/l). Indians had the highest blood glucose concentration followed by Chinese, Malays and other indigenous ethnic group (Lim *et al.*, 2000c). The particularly high prevalence of diabetes among the Indians in Malaysia reflects similar findings in Singapore

and elsewhere (Cutter *et al.*, 2001, Ramachandran *et al.*, 2001). In another study of 2,508 subjects in North-East Peninsular Malaysia, 10.5% were found to have diabetes mellitus and 16.5% have IGT. There was no difference in the prevalence of diabetes mellitus between males and females but the prevalence of IGT was higher in females (19.0%) than in males (11.5%). Subjects with diabetes mellitus were more obese (38.4%) than normal subjects (24.1%). They also had a higher prevalence of hypertension (12.9% versus 5.3%) and hypercholesterolemia (71.9% versus 57.0%) than normal subjects. Subjects with impaired glucose tolerance also had a higher prevalence of obesity (35.5% versus 24.1%), hypertension (9.0% versus 5.3%) and hypercholesterolemia (63.0% versus 57.0%) than normoglycemic subjects (Mafauzy *et al.*, 1999).

Cholesterol is one of the important modifiable risk factor for cardiovascular disease. There is a paucity of data on the prevalence of hypercholesterolemia locally. A national sample for second NHMS component of blood total cholesterol of 20,041 individuals aged 30 years and above found that 5% of the adult population had high blood cholesterol (blood cholesterol concentration ≥ 6.2 mmol/L), 15% was at the borderline high (blood cholesterol concentration 5.2-6.2 mmol/L) and 80% had blood cholesterol in the desirable range (blood cholesterol concentration ≤ 5.2 mmol/L). Malays had the highest prevalence of high blood cholesterol, followed by Indians, Chinese and other indigenous ethnic group. However, for all ethnic groups, the blood cholesterol concentration was low compared to Western populations and comparable to non-western populations such as China (Lim *et al.*, 2000b). This may be related to various factors such as genetic, cultural and other environmental factors. An earlier study on a smaller sample size done predominantly on

urban population showed that Indians ethnicity has the highest prevalence of hypercholesterolemia compared to Malays and Chinese (Zaraihan *et al.*, 1994).

Nutritional status is an important determinant of the health of the population. In assessing nutritional status, anthropometry is one of the key tools used. It comprises several types of body measurements including weight and height. Based on weight and height measurements, body mass index (BMI) is computed and is a commonly used indicator of adult nutritional status. Overweight and obesity are key determinants of non-communicable diseases such as hypertension, hypercholesterolemia, diabetes mellitus, and several types of cancer (Jia *et al.*, 2002, Jafar *et al.*, 2006). Many cross-sectional studies in Malaysia have reported on the problem of overweight and obesity in adults. The second NHMS component on body weight and height was conducted among 28,737 Malaysian adult populations aged 18 years and above found that the prevalence of overweight and obesity was 16.6% and 4.4% respectively (Ministry of Health, 1997). Prevalence of overweight among females (17.9%) was higher than that in males (15.1%). However, the prevalence of obesity among women (5.7%) was found to be twice that of men (2.9%). A cross sectional study of 2,284 subjects aged 20 years and over in nine districts of Kelantan found that the prevalence of overweight and obesity was 21.3% and 4.5% respectively. The overweight and obese were significantly younger than the underweight subjects. The prevalence of hypercholesterolemia (serum cholesterol >5.2 mmol/l) in underweight, overweight and obese subjects was 65.3%, 70.2% and 74.7%, respectively. IGT was found in 16.6% of the underweight, 21.6% of the overweight and 32.0% of the obese subjects. Diabetes mellitus was found in 7.9% of the underweight, 10.5% of the overweight and 6.7% of obese subjects. Ten percent of underweight, 13.2% of overweight and 23.3% of obese individuals

were hypertensive. This study suggested that the high prevalence of overweight and obesity in Kelantan was associated with adverse lipid and glucose metabolism as well as poor blood pressure control (Mohamad *et al.*, 1996). A study of 300 men and 300 women from Kuala Lumpur found that the prevalence of overweight (BMI > 21.5 kg/m² in men and > 20.5 kg/m² in women) to be highest among Malay men (44%) and Indian women (50%) in the 31 to 40 age group. However, in the older age group of 41 to 50, the situation was reversed with the highest percentage of Indian men (27%) and Malay women (33%) who were overweight. The prevalence of overweight among Chinese men and women was relatively much lower, being 4% and 7% respectively in the 31 to 40 years age group and 20% for both genders in the older age category (Jones, 1976). A study in 1988 showed that the difference in the prevalence of overweight between 300 Malays and Chinese men aged from 25 to 54 years from Kuala Lumpur was significant. Approximately 37% of the Malays were overweight (BMI 25 kg/m² to 30 kg/m²), compared to 21% among the Chinese. The prevalence of overweight among the Indians was also high at 32% (Teo *et al.*, 1988).

1.1.10 Changes of the sedentary lifestyle related to cardiovascular risk factors in Malaysia.

Cigarette smoking is known to be a strong predictive factor of cardiovascular in adults. The second NHMS conducted in Malaysia of 1996 found that the overall prevalence of smoking in adults over the age of 18 years was 24.8% with a prevalence of 49.2% in males and 3.5% in females (Haniza and Suraya, 1997). A study among 894 subjects from Sepang district in Selangor showed that the overall prevalence of smoking was 33.6%. Sixty-nine percent males compared to 3.9% of the females reported to have smoked at least once in their lifetime (Rampal and Narasimman, 2003).

Alcohol consumption is one of the lifestyle changes that intensely affect the development of many chronic diseases including cardiovascular diseases. The trend of alcohol consumption among Malaysian is rising and it is of growing concern. The national burden of alcohol consumption in Malaysia was first reported by the second NHMS in 1996 which revealed the prevalence of current drinkers among the non-Muslim adult population aged 18 years and above was 23.0%. Malaysians also reported to have started drinking at as early as 7 years of age. The average age at starting drinking was 22.3 years (Ministry of Health, 1997).

Unhealthy eating habits and decreased physical activity also showed some indication of how health could deteriorate if necessary measures with regard to lifestyle were neglected in daily life. There have been numerous nutritional and health status studies among the Malaysian adults and elderly. A study carried out in 2003 among 100 Malay adults from district of Selangor, aged 40 years and above indicated that rice, fish and vegetables were the foods consumed almost everyday by the majority of the subjects. Meat, dairy products and fruits were eaten once to three times per week. Food intake score for sugar and salt demonstrated that a majority of men and women consumed moderate amounts of these foods. The food habits of these adults were satisfactory. However, they exhibited an increasing trend towards blood pressure, high blood cholesterol and glucose with age. Furthermore, most subjects (74%) exercised twice to three times a week for 15 minutes for each exercise session and more women (82%) than men (66%) were spending this amount of time to exercise. In contrast 34% of men and 18% of women would extend between 30 to more 45 minutes of their time for exercise session. Some exercises which were undertaken and favoured included badminton, cycling, walking and static exercise